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EXAMINER	
GREENE, IVAN A	

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1619	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,159	PILGAONKAR ET AL.	
	Examiner	Art Unit	
	IVAN GREENE	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-9,11,14-19,21-25 and 27-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-9,11,14-19,21-25 and 27-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/09/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-32 are pending. Claims 5, 10, 12, 13, 20, 26 and 32 have been canceled by applicant. Claims 1-4, 6-9, 11, 14-19, 21-25, and 27-31 are presented for examination on the merits.

Priority

The effective US filing date of the instant application has been determined to be 02/10/2005 the filing date of the international application PCT/IB05/00330. The foreign priority date has been determined to be 02/11/2004, the filing date of Australian document 2004900661.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 11/09/2006, was filed after the mailing date of the first office action on the merits. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the Examiner.

Specification

The use of the following trademarks have been noted in this application:

- Amberlite® (p. 15, line 19)
- Sentry Polyox® (p. 17, table 1; p. 18, table 2; p. 20, table 4, p. 25, table 10)
- Methocel® (p. 17, table 1; p. 18 & 19, table 2; p. 22, table 7; p. 24, table 9)
- Gelucire® (p. 19, lines 9, 10, 13 & table 3; p. 20, table 4)
- Lutrol® (p. 19, line 8; p. 22, table 7)
- Natrosol® (p. 22, table 7)
- Primojel® (p. 22, table 7; p. 26, table 11; p. 26, table 11)

- Avicel® (p. 23, table 7; p. 25, table 11)
- Carbowax® (p. 23, table 8)
- Cekol® (p. 23, table 8; p. 24, table 9)
- Cremophor® (p. 24, table 9, line 9)
- Prosolve® (p. 24, table 9)

It should be capitalized or accompanied by an appropriate trademark symbol (e.g. ®, ™) wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claims 21 and 29 are objected to for the following informalities: the claims recite the word --pregelatinised-- should be spelled as "pregelatinized" (clam 21 line 6; claim 29 line 3). Appropriate correction is required.

Claim 3 is objected to because of the following informalities: the word "and" in lines 4 and 5 is unnecessary; the word "labour" should be spelled labor in line 5; the word "antifingal" should be spelled antifungal in line 5. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1, 2, 7, 9, 11, 15-19, 21, 24, 25 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point

out and distinctly claim the subject matter which applicant regards as the invention.

2. Regarding claim 1: the claim recites --active agents showing low bioavailability-- in line 3, however it is unclear what exactly is meant by "low bioavailability".

3. The term "sufficiently increased" in claim 2 is a relative term which renders the claim indefinite. The term "sufficiently increased" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what exactly the size of the dosage form should be increased to in order to provide retention of the dosage form in the stomach of a patient.

4. The term "prolonged time period" in claim 2 is a relative term which renders the claim indefinite. The term "prolonged time period" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear exactly how much time the dosage form should be retained in the patients stomach in order to gradually erode.

5. Claims 7 and 9 are rejected for reciting improper Markush language. Claims 7 and 9 recite --is selected from--. Claims 7 and 9 requires the addition of the word/phrase "the group consisting of". See MPEP § 2173.05(h) for more information.

6. Regarding claims 11, 15, 19 and 30, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

7. Claim 15-19 recites the limitation "hydrophilic polymer" in line 2. There is insufficient antecedent basis for this limitation in the claim.

8. Claim 19 is further rejected because it is unclear whether the phrase "about" is modifying the recited --10-- or --70-- or both.

9. Claim 21 contains the trademark/trade name Amberlite®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a polymeric ion exchange resin and, accordingly, the identification/description is indefinite.

10. Claim 24 is rejected because it is unclear whether the phrase "about" is modifying the recited --5-- or --90-- or both.

11. Claim 25 is rejected because it is unclear whether the phrase "about" is modifying the recited --10-- or --70-- or both.

12. Claim 30 is further rejected because it is unclear whether the phrase "about" is modifying the recited --0.25%-- or --10%-- or both; and it is unclear whether the phrase "about" is modifying the recited --0.5-- or --5.0%-- or both

13. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 30 recites the broad recitation --0.25% to 10%--, and the claim also recites --0.5 to 5.0%-- and --about 1%--, both of which are the narrower statements of the range/limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1, 3, 6-9, 11, 14-18, 21 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al. (WO 2001/022791 A2).

Applicant claims

Applicant claims a controlled release oral pharmaceutical composition comprising (a) a therapeutically effective amount of one or more pharmacological agents, (b) one or more solubilizers, (c) one or more biocompatible swelling agents, and (d) a swelling enhancer.

Prior Art

Singh et al. disclose controlled release compositions comprising nimesulide (title), an anti-inflammatory/analgesic drug (p. 2, line 9, instant claim 3). Singh et al. further disclose an example of their composition (Example 8, p. 18):

Example 8 Nimesulide CR + Cetirizine Bilayered Tablets

Nimesulide Layer		
(i) Nimesulide (micronized)	-	200 mg
(ii) Lactose	-	106.5 mg
(iii) Polyoxyl 40 Hydrogenated Castor Oil	-	2.0 mg
(iv) Hydroxypropylmethylcellulose	-	31.5 mg
(v) Magnesium Stearate	-	2.0 mg
(vi) Colloidal Silicon Dioxide	-	2.0 mg
Cetirizine Layer		
(vi) Colloidal Silicon Dioxide	-	2.0 mg
(vii) Cetirizine Dihydrochloride	-	10.0 mg
(viii) Lactose	-	105.0 mg
(ix) Microcrystalline Cellulose	-	25.0 mg
(x) Starch	-	5.0 mg
(xi) Croscarmellose Sodium	-	3.0 mg
(xii) Magnesium Stearate	-	2.0 mg

wherein the active is (i) nimesulide, the solubilizer is (iii) polyoxy 40 hydrogenated castor oil, the biocompatible swelling agent is (x) starch, and the swelling enhancer is (ix) microcrystalline cellulose (instant claims 1 & 21). Singh et al. disclose, in Example 8, the lipophilic nonionic surfactant solubilizer (iii) polyoxy 40 hydrogenated castor oil (instant claims 6-9). Examiner notes the ratio of solubilizer to drug is 2.0/200 = 0.01 which is greater than 1/20 = 0.05 and less than 20 (instant claim 11). Singh et al.

disclose, in Example 8, the ingredient (iv) hydroxypropylmethylcellulose which is a cellulosic polymer swelling agent (instant claims 14 & 15); and is about 6.3% (31.5/496 X 100) of the total composition (instant claim 18). The swelling enhancer, microcrystalline cellulose, in the above example is about 5% (25/469 X 100) of the total composition (instant claim 24).

Singh et al. further disclose an example of their composition (Example 5, p. 16):

Example 5 Coated capsule type

(i) Nimesulide (micronized)	-	200 mg
(ii) Microcrystalline Cellulose	-	66.4 mg
(iii) Lactose	-	70 mg
(iv) Polyvinyl Pyrrolidone	-	7 mg
(v) Magnesium Stearate	-	3.9 mg
(vi) Ethyl Cellulose	-	20 mg
(vii) Polyethylene Glycol	-	0.7 mg
(viii) Alcohol : Dichloromethane (1 : 2)	-	q.s (Lost in processing)
(ix) Empty Gelatin Capsule (Size '1')		

wherein the active is (i) nimesulide, the solubilizer is (vii) polyethylene glycol (synonymous with poly(ethylene oxide), instant claims 16 & 17), the biocompatible swelling agent is (vi) ethyl cellulose, and the swelling enhancer is (ii) microcrystalline cellulose (instant claim 1).

2. Claims 27-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Doshi et al. (US 7,157,100 B2, prior publication as US 2003/0232081 A1).

Applicant claims

Applicant claims a pharmaceutical dosage form in the form of an expanding multi-layered system comprising a first layer property having at least one active pharmaceutical ingredient with an immediate release layer; and a second layer having at least one active pharmaceutical ingredient with a sustained release property.

Prior Art

Doshi et al. disclose a pharmaceutical composition for controlled drug delivery comprising an anti-bacterial active ingredient, ofloxacin; and having an immediate release first layer and a controlled release second layer (col. 4, lines 47-55; Example 1 below). Doshi et al. disclose the example comprising (Example 1; col. 9, lines 5-27):

1.	Ingredients of Immediate layer	
	Ofloxacin	7.0
	Microcrystalline cellulose	1.5
	Anhydrous Colloidal Silica	1.0
	Color iron oxide yellow	1.0
	Sodium starch glycolate	1.0
	Magnesium stearate	0.5
2.	Ingredients of Controlled release layer	
	Ofloxacin	63.0
	Methyl Cellulose (Viscosity 80,00–120000 cp) available under the trademark Methocel ® K 100 M	6.0
	Methyl Cellulose (Viscosity 3000–5600 cp) available under the trademark Methocel ® K 4 M	4.0
	Sodium bicarbonate	7.0
	Lactose	4.0
	Talc	1.0
	Magnesium stearate	1.0
3.	Coating	
	Methacrylic acid copolymer available under trademark Eudragit ® L 100	2.0

wherein the composition consists of 1% (1 mg / 100 mg X 100) of the disintegrating agent, sodium starch glycolate (Example 1; col. 9, lines 5-27, instant claims 27, 29 &

30). Examiner notes the ratio of the active in the first layer to the active in the second layer is 7/63 which equal to 10/90 (instant claim 28).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 2-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (WO 2001/022791 A2) and Doshi et al. (US 7,157,100 B2, prior publication as US 2003/0232081 A1) and Flashner-Barak et al. (US 6,881,420 B2).

2. Examiner notes the claims, rejected above as being anticipated (claims 3, 6-9, 11, 14-18, 21, 24 and 28-30), are further rejected in the unanticipated embodiments as being obvious.

Applicant claims

Applicant claims a controlled release oral pharmaceutical composition comprising (a) a therapeutically effective amount of one or more pharmacological agents, (b) one or more solubilizers, (c) one or more biocompatible swelling agents, and (d) a swelling enhancer. Applicant further claims the controlled release composition swells in the presence of gastric fluid such that the dosage form is retained until it erodes in the stomach of the patient. Applicant further claims a process for preparing a pharmaceutical composition comprising the steps of solubilizing an active pharmaceutical ingredient with one or more solubilizing agents and incorporating said solubilized active agent in a gastro retentive matrix having one or more swelling agents and one or more swelling enhancers.

Determination of the scope and content of the prior art (MPEP 2141.01)

Singh et al. teach controlled release compositions comprising nimesulide (title), an anti-inflammatory/analgesic drug (p. 2, line 9, as discussed above). Singh et al. further teach their composition may be used in combination with another drug to have a synergistic activity (p. 11, lines 23-25) and the other drug may be the anti-asthmatic salbutamol (p. 12, line 6).

Doshi et al. teaches a floating bilayer tablet which is retained in the stomach of the patient (col. 3, lines 65-67; col. 4 lines 1-4; as discussed above).

Flashner-Barak et al. teach compositions and dosage forms for gastric delivery of active agent(s) (title). Flashner-Barak et al. further teach a gastric retention vehicle composition comprising a hydrogel, wherein the dosage form expands upon

contact with gastric fluid and is retained in the patients stomach for a prolonged period of time (col. 6, lines 35-42). Flashner-Barak et al. further teach the gastric retention vehicle composition optionally also includes a superdisintegrant, for example, cross-linked polyvinylpyrrolidone (col. 9, lines 42-43 & 49-50). Flashner-Barak et al. further teach the excipients which include a lubricant (solubilizer), for example, hydrogenated castor oil, hydrogenated vegetable oil, and polyethylene glycol (col. 18, lines 8-15). Flashner-Barak et al. further teach the swelling agents hydroxypropyl methylcellulose (col. 8, line 64).

Flashner-Barak et al. further teach the expanding tablets may be prepared by dry granulation or wet granulation, followed by compaction of the resulting tableting composition (col. 10, lines 50-54). Flashner-Barak et al. further teach the examples wherein the all of the excipients except magnesium stearate are mixed simultaneously and thoroughly blended by hand before tableting in tableting machine (col. 19, lines 39-40 & 45-46; Example 1). Flashner-Barak et al. further teach the tablets of example 1 were added to simulated gastric fluid to test the degree of swelling (col. 20, lines 1-25; Table 2).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

The difference between the rejected claims and Singh et al. is that Singh et al. do not teach a composition(s) which float in the stomach, the active agent(s) of instant claim 4, the cross-linked polyvinylpyrrolidone of instant claims 22 and 23, the method of instant claim 31 or the percent(s) claimed in instant claims 19 and 25.

The deficiency in the dosage form which swells and floats in the stomach until it erodes over a prolonged time period is cured by the teachings teachings of Flashner-Barak et al. Doshi et al. further teaches a floating bi-layer tablet with an immediate and controlled release of active agent.

Regarding the active agent of instant claim 4: Singh et al. teach the active agent salbutamol, however, they do teach an example such that it would be anticipated. However it would be obvious to choose salbutamol in addition to the nimesulide which is taught.

The deficiency in the cross-linked polyvinylpyrrolidone of instant claims 22 and 23 is cured by the teachings of Flashner-Barak et al.

Regarding the method of instant claim 31, Flashner-Barak et al. clearly teach the excipients including a solubilizer, a swelling agent, and a swelling enhancer, however they do not teach a single example contain each said excipient. Furthermore, Flashner-Barak et al. teach the method of mixing all excipients and tableting into a gastro retentive matrix.

Regarding the percent(s) claimed in claims 19 and 25, neither of the references teaches adding the active ingredients in the amounts claimed by Applicant. The amounts of specific ingredients in a composition are clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for a skilled artisan to determine the optimal amount of each ingredient to add in order

to best achieve any of the desired results cited in claims 19 and 25. Thus, in the absence of some demonstration of unexpected results from the claimed parameters, this optimization of ingredients would have been obvious at the time of Applicant's claimed invention.

Finding of prima facie obviousness

Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of Singh et al. and Doshi et al. with the teachings of Flashner-Barak et al., and produce the instant invention because they each teach controlled release formulations. It is prima facie obvious to combine compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, i.e. a controlled release formulation. See MPEP 2144.06. One of ordinary skill in the art would have been motivated to do this because the controlled release formulation of Doshi et al. and/or Flashner-Barak et al. would provide an improved strategy for affecting the controlled release of an active pharmaceutical ingredient.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Conclusion

Claims 1, 3, 6-9, 11, 14-18, 21, 24 and 28-30 are rejected under 35 U.S.C. 102(b) and claims 2-31 are rejected under 35 U.S.C. 103(a). No claims allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to IVAN GREENE whose telephone number is (571)270-5868. The examiner can normally be reached on Monday through Thursday 7AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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